

REMARKS/ARGUMENTS

Claims 1-23 and 25-26 are pending. Claims 1, 4 and 5 have been amended for clarity. Claim 11 has been amended to correct a typographical error in the last formula. Accordingly, the Applicants believe that no new matter has been introduced.

Rejection—35 U.S.C. 112, second paragraph

Claim 11 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The Applicants thank Examiner Keys for detecting this typographical error, which has now been corrected.

Rejection—35 U.S.C. 103

Claims 1-10 and 12-26 were rejected under 35 U.S.C. 103(a) as being unpatentable over Murata, J. Am. Chem. Soc. 120:7117, in view of Bierschenk et al., U.S. Patent 5,093,432. The present invention is not disclosed or suggested by the cited prior art for the following reasons.

The Official Action assumes that compounds having a vic-dichloro structure ( $\text{CH}_2\text{ClCHCl-}$ ) can be fluorinated in the same manner as other types of chlorinated hydrocarbons. The Applicants disagree for the following reasons.

The fluorination reactions of Bierschenk et al. involve fluorination of compounds where the chlorine atom is attached to a primary carbon atom. Bierschenk et al. disclose fluorination of chlorinated compounds in Examples 16-19, 43-47, 48 (col. 31, line 54-col. 32, line 1), 51, 62 and 64. However, all these examples involve fluorination of compounds having a chlorine atom attached to a primary carbon atom (e.g.,  $-\text{CH}_2\text{Cl} \rightarrow \text{CF}_2\text{Cl}$ ). Therefore, there is no suggestion or reasonable expectation of success provided by the cited

art which would have motivated one of ordinary skill in the art to practice the present invention, which involves the formation in a good yield of a compound of formula (II) having a vic-dichloro structure ( $\text{CF}_2\text{ClCF}\underline{\text{Cl}}$ -) where the chlorine atom is attached to a secondary or tertiary carbon atom (the underlined chlorine atom in the above formula).

It is well-known to those skilled in the art that a chlorine atom attached to a primary carbon atom is relatively stable during fluorination, but that a chlorinated atom attached to a secondary or tertiary carbon atom is vulnerable to rearrangement or elimination during fluorination, see Adcock et al., J. Org. Chem. 49:2719-2733 (1984)(attached), page 2720, col. 1, lines 6-*et seq.* below Table 1. These rearrangements result in production of products that do not correspond to the original unfluorinated compound, because the chlorine atoms are rearranged.

Similarly, there is no reasonable expectation of success in Bierschenk for the present invention as directed to fluorination of a chlorine atom attached to a tertiary carbon atom as in  $\text{CHCl}=\text{CCl}$ - (see  $\text{R}^{\text{H1}}$  in Claim 1). Such a chlorine atom attached to a tertiary carbon atom is also vulnerable to rearrangement during fluorination, as disclosed by Adcock et al., J. Org. Chem. 49:2719-2733 (1984). Moreover, Bierschenk et al. do not disclose fluorination of any compounds having a chlorine atom attached to a tertiary carbon atom. Therefore, this document cannot suggest or provide a reasonable expectation of success for the present invention where a compound (I) where  $\text{R}^{\text{H1}}$  is  $\text{CClX}_4=\text{CCl}$ - can be fluorinated without rearrangement of the chlorine atom attached to the tertiary carbon atom.

Furthermore, with respect to claim 2, a compound (I) having a molecular weight higher than a certain level is not likely to undergo a decomposition reaction in a gas phase during fluorination. When a compound (I) has a certain level of fluorine content, the compound (I) dissolves well in the liquid phase, and therefore, formation of a heterogeneous reaction system and consequential decomposition of the compound (I) through the heat

generated by the heterogeneous reaction can be prevented. As the prior art does not suggest nor provide a reasonable expectation of success for the present invention, the Applicants respectfully request that this rejection be withdrawn.

**CONCLUSION**

In view of the above amendments and remarks, the Applicants respectfully submit that this application is now in condition for allowance. Early notification to that effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, P.C.  
Norman F. Oblon

A handwritten signature in black ink, appearing to read "Thomas Cunningham", written in a cursive style.

Thomas Cunningham  
Registration No. 45,394

Customer Number

**22850**

Tel: (703) 413-3000  
Fax: (703) 413 -2220  
NFO/TMC/cja

J. Org. Chem. 1984, 49, 2719-2723

2719

## Aerosol Direct Fluorination: Alkyl Halides. 2. Chlorine Shifts and the Stability of Radicals

James L. Adcock\* and William D. Evans

Department of Chemistry, University of Tennessee, Knoxville, Tennessee 37996-1600

Received November 1, 1983

Unlike alkyl bromides and iodides, alkyl chlorides are shown to be stable to direct fluorination, even under ultraviolet irradiation, at temperatures of 30 °C and below. Although less reactive than the bromides and iodides, *F*-alkyl chlorides may be derivatized, presenting another example of direct fluorination-survivable functionality. High (63%) to moderate (32%) isolated yields of the analogous perfluoroalkyl chlorides can be synthesized by aerosol direct fluorination of 1-chloropropane, 1-chlorobutane, 1-chloro-2-methylpropane, 1-chloro-3-methylbutane, 1-chloro-2-methylbutane, and chlorocyclopentane with generally less than 20% C-C bond cleavage. Tertiary alkyl chlorides generally undergo intramolecular 1,2-chloride shifts in the earliest stages of reaction in a manner characteristic of  $\beta$ -chloro radicals forming principally primary *F*-alkyl chlorides. Thus 2-chloro-2-methylpropane produces 1-chloro-*F*-2-methylpropane (47%), and 2-chloro-2-methylbutane produces a 16:6:3:1 ratio of 1-chloro-*F*-2-methylbutane, 1-chloro-*F*-3-methylbutane, and 2-chloro-*F*-3-methylbutane, respectively, in 32% combined yield. Secondary alkyl chlorides undergo a similar but incomplete rearrangement producing mixtures of primary and secondary *F*-alkyl chlorides. Thus 2-chloropropane produces a 2:1 mixture of 2-chloro-*F*-propane and 1-chloro-*F*-propane in 50% combined yield; 2-chlorobutane produces a 1:1.5 mixture of 2-chloro-*F*-butane and 1-chloro-*F*-butane in 84% combined yield, and 3-chloropentane produces a 2:3:1 mixture of 3-chloro-*F*-pentane, 2-chloro-*F*-pentane, and 1-chloro-*F*-pentane, respectively, in a combined yield of 30%. Because secondary alkyl chlorides partially rearrange but primary alkyl chlorides do not rearrange at all on fluorination, doubt is cast on the postulate that the intermediate radicals are equilibrating.

The fluorination of compounds with survivable functionality permits the preparation of fluorinated compounds with preselected sites for further reaction. The survivability of acyl fluorides,<sup>1,2</sup> ethers,<sup>3,4</sup> ketals,<sup>4</sup> and, to a lesser extent, esters<sup>1</sup> and amines<sup>3,5</sup> to elemental fluorine attack are well documented in the literature. More recently reliable ketone direct fluorinations have been documented<sup>7</sup> although isolated cases of direct fluorination syntheses of ketones, albeit in poor yields, have been noted previously.<sup>8</sup> The stability of perfluoroketones to photochemically finished aerosol direct fluorination is remarkable given their known photolability.<sup>9</sup>

Perhaps the most useful monovalent substituent groups on perfluorocarbons are the iodides.<sup>10</sup> Perfluoroalkyl bromides are less reactive and are rarely used if the iodides are available. However neither of these substituents will survive attack by elemental fluorine. Until the recent aerosol direct fluorination of neopentyl chloride the useful survivability of a chloro group was in doubt.<sup>11</sup> Many previous attempts to directly fluorinate alkyl chlorides resulted in extensive fragmentation, chlorine loss, and significant free radical chlorination competing with fluorination.<sup>12-19</sup> For example, the reaction of elemental fluorine

with 1,2-dichloropropane at 100–200 °C gave large amounts of CF<sub>4</sub>, C<sub>2</sub>F<sub>6</sub>, and C<sub>3</sub>F<sub>8</sub> as well as small amounts of 1,2-dichloro-*F*-propane, 1,3-dichloro-*F*-propane, and materials containing three or more chlorines.<sup>20</sup> The ease with which the C-Cl bond was cleaved and the degree of free radical chlorination giving rise to polychlorinated products were in retrospect obviously a result of the high temperatures involved. In contrast to the above works this work demonstrates the exceptional stability of a number of chloroalkanes toward fission of the C-Cl bond by photochemically finished aerosol direct fluorination. The predictable occurrence of 1,2-chloride shifts giving rearranged products in some instances has been studied systematically as well.

### Results and Discussion

A previous contribution in the area of aerosol direct fluorination of alkyl halides showed that alkyl chlorides underwent exclusively free radical attack by elemental fluorine.<sup>11</sup> This is in contrast to the carbocation generation which occurred, at least initially, when alkyl bromides were subjected to aerosol direct fluorination.<sup>11</sup> The extremely low degree of C-Cl bond fission occurring in the aerosol fluorination of neopentyl chloride prompted us to look more extensively into the aerosol direct fluorination of other alkyl chlorides as a means by which preselected survivable sites for subsequent reaction could be incorporated into organic molecules prior to their fluorination.

The aerosol direct fluorination process has been described in detail elsewhere.<sup>4,7</sup> The process is a steady-state flow process in which a hydrocarbon vapor is condensed onto a sodium fluoride preaerosol and then subjected to attack by a 50–100% excess over the stoichiometric amount of elemental fluorine at low (2–5%) concentration in helium at low (–70 to 0 °C) temperatures in the dark.

- (1) Adcock, J. L.; Lagow, R. J. *J. Am. Chem. Soc.* 1974, 96, 7588.
- (2) Adcock, J. L.; Beh, R. A.; Lagow, R. J. *J. Org. Chem.* 1975, 40, 3271.
- (3) Adcock, J. L.; Lagow, R. J. *J. Org. Chem.* 1974, 39, 3617.
- (4) Adcock, J. L.; Horita, K.; Reak, E. B. *J. Am. Chem. Soc.* 1981, 103, 6937.
- (5) Adcock, J. L.; Catsikis, B. D.; Thompson, J. W.; Lagow, R. J. *J. Fluorine Chem.* 1976, 7, 197.
- (6) Bishop, B. C.; Hynes, J. B.; Bigelow, L. A. *J. Am. Chem. Soc.* 1964, 86, 1927.
- (7) Adcock, J. L.; Robin, M. L. *J. Org. Chem.* 1983, 48, 2437.
- (8) Holub, P. F.; Bigelow, L. A. *J. Am. Chem. Soc.* 1950, 72, 4879.
- (9) Giacometti, G.; Okabe, H.; Price, S. J.; Steacie, E. W. R. *Can. J. Chem.* 1960, 38, 104.
- (10) Banks, R. E. "Fluorocarbons and Their Derivatives", 2nd ed.; Macdonald: London, 1970; p 79, 102.
- (11) Adcock, J. L.; Evans, W. D.; Heller-Grossman, L. *J. Org. Chem.* 1983, 48, 4952–4957.
- (12) Miller, W. T.; Koch, S. D. *J. Am. Chem. Soc.* 1957, 79, 3084.
- (13) Ruff, O.; Keim, R. Z. *Anorg. Allg. Chem.* 1931, 201, 245.
- (14) Bockmüller, W. *Justus Liebig's Ann. Chem.* 1933, 506, 20.
- (15) Miller, W. T.; Calfee, J. D.; Bigelow, L. A. *J. Am. Chem. Soc.* 1937, 59, 198.
- (16) (a) Calfee, J. D.; Bigelow, L. A. *J. Am. Chem. Soc.* 1937, 59, 2072.
- (b) Young, D. S.; Fukuhara, N.; Bigelow, L. A. *Ibid.* 1940, 62, 1171.
- (17) Calfee, J. D.; Fukuhara, N.; Young, D. S.; Bigelow, L. A. *J. Am. Chem. Soc.* 1940, 62, 267.
- (18) Hadley, E. H.; Bigelow, L. A. *J. Am. Chem. Soc.* 1940, 62, 3302.
- (19) Miller, W. T. *J. Am. Chem. Soc.* 1940, 62, 341.
- (20) Schmeisser, M.; Ehlers, K. P.; Sartori, P. *Angew. Chem., Int. Ed.* 1967, 6, 627.

2720 J. Org. Chem., Vol. 49, No. 15, 1984

Adcock and Evans

Table I. Aerosol Direct Perfluorinations of Chloroalkanes

starting compd	product 1	effluent concn, %	yield, <sup>a</sup> %	product 2	effluent concn, %	yield, %	product 3	effluent concn, %	yield, %
1-chloro-propane	1-chloro-F-propane	85	63						
1-chlorobutane	1-chloro-F-butane	60.2	42.4	F-butane					
1-chloro-2-methyl-propane	1-chloro-F-2-methylpropane	76.4	41	F-2-methyl-propane	15.8		b hydryl-1-chloro-F-butanes		b
1-chloro-3-methyl-butane	1-chloro-F-3-methylbutane	67	32	F-2-methyl-butane	19				
1-chloro-2-methyl-butane	1-chloro-F-2-methylbutane	55	39	F-2-methyl-butane	19				
2-chloro-2-methyl-propane	1-chloro-F-2-methylpropane	80.4	47						
2-chloro-2-methyl-butane	1-chloro-F-2-methylbutane	48.1	c	1-chloro-F-3-methylbutane	17.0	e	2-chloro-F-3-methylbutane	2.7	c
2-chloro-propane	2-chloro-F-propane	52	d	1-chloro-F-propane	28	d			
2-chlorobutane	2-chloro-F-butane	30	e	1-chloro-F-butane	48	e			
3-chloro-pentane	3-chloro-F-pentane	30	f	2-chloro-F-pentane	45	f	1-chloro-F-pentane	15	f
chlorocyclopentane	chloro-F-cyclopentane	49.5	40.2	F-cyclopentane	12.5		F-pentane <sup>g</sup>	12.5	

<sup>a</sup> Yields are based on total starting compound injected that are not corrected for recovered unreacted starting material collected at the close of the reaction. <sup>b</sup> Combined yield 6.9%. <sup>c</sup> Combined yield 31.8%. <sup>d</sup> Combined yield 50%. <sup>e</sup> Combined yield 34%. <sup>f</sup> Combined yield 30%. <sup>g</sup> Three isomeric chloro-F-pentanes make up 15.5% of effluent.

The partially (50–70%) fluorinated hydrocarbons are then subjected to ultraviolet irradiation at ambient fluorine concentrations to remove residual hydrogen atoms. Partial fluorination runs are conducted under precise stoichiometric control usually without photochemical finishing.

Primary alkyl chlorides such as *n*-propyl chloride, *n*-butyl chloride, and isobutyl chloride show exceptional stability to both elemental and photochemically generated atomic fluorine (Table I). In contrast, the aerosol direct fluorination of tertiary alkyl chlorides results in a 1,2-chloride shift giving primary perfluoroalkyl chlorides (Table I). For example in the aerosol fluorination of *tert*-butyl chloride, complete conversion to *F*-isobutyl chloride is observed. No fluorinated tertiary chlorine products were observed. A second reaction with only 6 mmol/h of fluorine with 8 mmol/h *tert*-butyl chloride and without photofinishing gave unreacted *tert*-butyl chloride (30%), 1-chloro-2-fluoro-2-methylpropane (30%), 1-chloro-2,3-difluoro-2-methylpropane (20%); and 1-chloro-1,2-difluoro-2-methylpropane (2%) plus more highly fluorinated material (15%). The only tertiary chloride that was observed occurred on unreacted starting material. No free chlorine was observed, nor were any products found to contain more than one chlorine. This reaction shows that the chloride shift occurs on radical formation early in the fluorination. Chlorine fission due to photolysis or fluorine displacement apparently does not occur with observable significance.

In the aerosol fluorination of *tert*-amyl chloride (2-chloro-2-methylbutane, Table I) three rearranged perfluoroalkyl chlorides were collected. The relative, near statistical, proportions of 1-chloro-F-2-methylbutane (43.1%) and 1-chloro-F-3-methylbutane (17.0%), while only a trace of 2-chloro-F-3-methylbutane (2.7%) was collected, shows that multiple 1,2-chloride shifts occur readily during perfluorination. Perfluoro-*tert*-amyl chloride was not produced.

Secondary alkyl chlorides show intermediate stability when fluorinated giving both primary and secondary

perfluoroalkyl chlorides (Table I). Evidence for multiple 1,2-chloride shifts are seen again in the perfluorination of 3-chloropentane.

These results are for the most part supported by literature accounts of rearrangements associated with free radical reactions. For example, Skell, Allen, and Gilmour observed that chlorination of 2-bromopropane and 2-bromo-2-methylpropane produced 1-bromo-2-chloropropane and 1-bromo-2-chloro-2-methylpropane, respectively.<sup>21</sup> These findings indicated complete rearrangement. An initial hydrogen abstraction from one of the methyl groups leading to a primary radical was immediately followed by a 1,2-bromide migration to form a more stable tertiary radical that then added chlorine to form the rearranged products. Juneja and Hodnett observed the same 1,2-bromide shift in the chlorination of 2-bromo-2-methylpropane as did Skell et al.<sup>22</sup> They also observed that no rearrangement occurred in the chlorination of 1-bromo-2-methylpropane. The latter rearrangement would not be expected to occur as it would involve forming a primary radical from a tertiary radical. Formation of a tertiary radical is also statistically unfavorable.

Wiley et al. noted the isomerization of 1-chloropropane to 2-chloropropane during radiolysis but not the reverse reaction.<sup>23</sup> This seeming contradiction was reinvestigated by Benson and Willard, who observed that this reaction was catalyzed by hydrogen chloride and that the hydrogen atom exchanges, not the chlorine atom.<sup>24</sup> Mayo postulated that an equilibrium between secondary and primary radicals could explain this rearrangement.<sup>25</sup> If the reactions of these radicals require little or no activation energy, the

(21) Skell, P. S.; Allen, R. G.; Gilmour, N. D. *J. Am. Chem. Soc.* 1961, 83, 504–5.

(22) Juneja, P. S.; Hodnett, E. M. *J. Am. Chem. Soc.* 1967, 89, 5685–7.

(23) Wiley, R. H.; Miller, W.; Jarboe, C. H.; Harrell, J. R.; Parish, D. *J. Radiat. Res.* 1960, 13, 479–88.

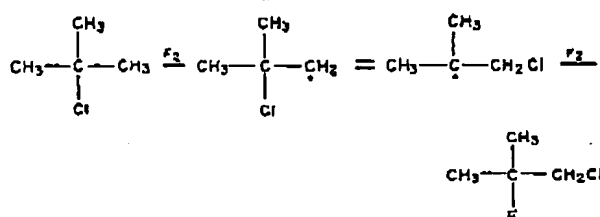
(24) Benson, H. L., Jr.; Willard, J. E. *J. Am. Chem. Soc.* 1961, 83, 4672–3.

(25) Mayo, F. R. *J. Am. Chem. Soc.* 1962, 84, 3964–6.

## Aerosol Direct Fluorination

J. Org. Chem., Vol. 49, No. 15, 1984 2721

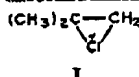
Scheme I



products will conform to the more stable radical. However, if the reactions of these radicals require a large activation energy and are therefore relatively difficult, then the products will conform to those derived from the minor proportions of the less stable, but more reactive radical. In this way the seeming contradiction is resolved; i.e., only the more reactive radicals formed by radiolysis, C-H bond fission, will react with HCl to produce the observed product because of the relatively high activation energy required.

The above postulate would also explain why products derived from the interactions of intermediate free radicals with fluorine molecules, a low activation energy process, should predominately correspond to those derived from the more stable radicals. Other free radical rearrangements involving 1,2-chloride shifts have been reviewed by Freidina.<sup>26</sup>

When a 1:2 molar ratio of *tert*-butyl chloride to fluorine aerosol fluorination was carried out, 1-chloro-2-fluoro-2-methylpropane was the major product observed. This suggests a mechanism (Scheme I) similar to that observed by Skell et al. in which initial H abstraction from a methyl group results in a rapid 1,2-chloride shift to produce a more stable tertiary radical.<sup>21</sup> This could occur by the formation of a bridged radical intermediate (I) that would open

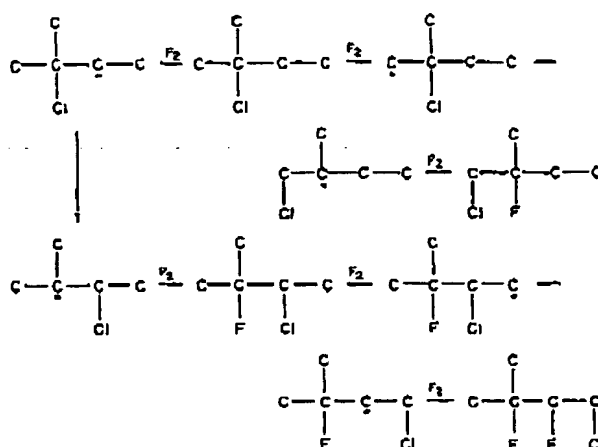


preferentially to the more stable tertiary radical.<sup>27</sup> If Mayo's postulate is general, the concentration of the tertiary radical would far exceed that of the primary radical giving the observed primary F-alkyl chloride. This postulate also explains the lack of rearrangements encountered during the fluorination of primary alkyl chlorides having  $\alpha$  tertiary hydrogens.

In the analogous fluorination of *tert*-amyl chloride, the tertiary chlorine can rearrange from a primary to a tertiary radical by a 1,2-chloride shift giving the primary F-alkyl chloride. However, the tertiary chloride can also rearrange by a 1,2-chloride shift giving a secondary chloride if the initial radical is formed by H abstraction at the methylene group. The secondary chloride can subsequently rearrange by a second 1,2-chloride shift giving the other possible primary alkyl chloride, 1-chloro-F-3-methylbutane, if a subsequent hydrogen abstraction by fluorine occurs on the 3-methyl group adjacent to the methylene group (Scheme II). This final shift would occur, however, only if the 3-methyl group has not been previously fluorinated.

The partial rearrangement of secondary alkyl chlorides during fluorination can also be rationalized by Mayo's postulate.<sup>25</sup> However in the case of equilibrium between primary and secondary alkyl radicals, the concentration of secondary radical would not be so predominant nor

Scheme II



would their reactivity differ as much. The more similar concentrations would therefore result in a mixture of products representing both rearranged and unrearranged products. The problem with Mayo's rationalization is that it should work in reverse; i.e., when primary alkyl chlorides are fluorinated, some secondary alkyl chloride should be isolated. Since this does not occur, there must be kinetic and/or other effects operating. This observation certainly casts some doubt on Mayo's postulation and a more careful look at the problem is indicated.

## Experimental Section

The basic aerosol fluorinator design and a basic description of the process are presented elsewhere.<sup>27</sup> Detailed parameters for reactor variables are given in Table II. Workup of products following removal of the hydrogen fluoride formed during the fluorination consisted of vacuum line fractionation, infrared assay of fractions, and gas chromatographic separation of components using either a 7 m  $\times$  3/8 in. 13% Fluorosilicone QF-1 (Analabs) stationary phase on 60-80 mesh, acid-washed, Chromosorb p conditioned at 225 °C (12 h) or a 4 m  $\times$  3/8 in. 10% SE-52 phenyl-methyl silicone rubber on 60-80 mesh, acid-washed, Chromosorb p conditioned at 250 °C (12 h). Following gas chromatographic separation (Bendix Model 2300, subambient multicontroller) all products of "significance" were collected, transferred to the vacuum line, assayed, and characterized by vapor-phase infrared spectrophotometry, PE1330, electron impact (70 eV) and chemical ionization (CH<sub>4</sub> plasma) mass spectrometry (Hewlett-Packard GC/MS, 5710A GC, 5980 A MS, 5934A Computer), and <sup>1</sup>H and <sup>19</sup>F nuclear magnetic resonance (JEOL FX90Q, omniprobe) in CDCl<sub>3</sub> with 1% CFCl<sub>3</sub> internal standard.

**Aerosol Fluorination of *n*-Propyl Chloride.** 1-Chloropropane (Matheson) has a vapor pressure at -45 °C such that a helium flow of 75 mL/min produces a throughput of 0.24 g/h (3.0 mmol/h). A 2-h run produced 0.909 g of crude material after fractionation. Separation isothermally at -20 °C on the SE-52 column gives 1-chloro-F-propane (85%) at retention time of 6 min (*t*<sub>R</sub> = 5 min). This corresponds to a 63% yield based on theoretical throughput. The IR spectrum matches that published.<sup>28</sup>

**Aerosol Fluorination of Isopropyl Chloride.** 2-Chloropropane (Eastman) has a vapor pressure at -45 °C such that a helium flow of 75 mL/min produces a throughput of 0.31 g/h (4.0 mmol/h). A 2.5-h run produced 1.2393 g of crude product after fractionation. Separation isothermally at -20 °C on the SE-52 column gives an unresolved peak (80%) (*t*<sub>R</sub> = 6 min). A second separation on the QF-1 column a broad peak (80%) (*t*<sub>R</sub> = 18 min). This mixture corresponds to 48.5% of the calculated yield. The IR spectrum shows a 1:2 mixture of 1-chloro-F-propane and 2-

(26) Freidina, R. Kh. *Adv. Free Radical Chem.*, 1965, 1, 211-278.(27) Kochi, J. K., Ed. *Free Radicals*; Wiley: New York, 1973; Vol. 2, Chapter 26, pp 829-832.(28) Hauptschein, M.; Nodiff, E. A.; Grosse, A. V. *J. Am. Chem. Soc.* 1952, 74, 1347.

Table II. Typical Aerosol Fluorination Reaction Parameters<sup>a</sup>

starting compd	fluorine flow, ml/min		helium diluent, ml/min		reaction temp, °C				main helium carrier, ml/min	hydrocarbon throughput, mmol/h (the carrier)	overall <sup>h</sup> stoichiometry, $\text{helium}:\text{F}_2$	% $\text{F}_2$ concn, final stage	run time, <sup>a</sup> h	product <sup>d</sup> effluent concn % collected	product <sup>d</sup> yield, % theor
	reactor	mod.	1	2	mod.	1	2	mod.							
n-propyl chloride	15	15	80	80	-40	-30	0	1000	3.0 (76)	1:25	2.4	65	65	63	
isopropyl chloride	20	20	80	80	-40	-30	0	800	4.0 (76)	1:25	3.9	75	~80	59	
n-butyl chloride	20	20	80	80	-45	-30	10	1000	3.4 (48)	1:42	4.4	60	60.2	42.2	
isobutyl chloride	20	20	80	80	-45	-30	10	1000	2.4 (50)	1:54	3.2	66	76.4	41.2	
sec-butyl chloride	19	19	76	76	-45	-30	10	1000	2.8 (83)	1:46	4.5	61	72.8	32.8 <sup>f</sup>	
tert-butyl chloride	20	20	70	70	-40	-30	10	1000	3.0 (13)	1:46	4.7	63	80.4	46.5 <sup>f</sup>	
tert-butyl chloride	2.5	2.5	70	70	-45	-30	10	800	3.0 (13)	1:2	0.3	91	h		
1-chloro-3-methylbutane	20	20	80	80	-40	-35	0	1000	3.0 (12)	1:40	4.5	62	67	32	
1-chloro-2-methylbutane	20	20	80	80	-40	-35	0	1000	3.0 (12)	1:40	4.5	62	66	39	
2-chloropentane	20	20	80	80	-45	-30	10	1000	1.2 (20)	1:172	4.5	62	80	31 <sup>g</sup>	
tert-amyl chloride	20	20	80	120	-40	-30	10	800	2.6 (53)	1:44	4.5	74	52.8	31.8	
cyclopentyl chloride	20	20	80	80	-40	-30	10	1000	2.0 (135)	1:73	4	57	49.5	40.2	

<sup>a</sup> See ref 4 and 7 for significance, meaning of parameters (mod. = module). <sup>b</sup> 1.0 mL/min  $\text{F}_2$  delivers 2.44 mmol/h of  $\text{F}_2$ . <sup>c</sup> Reactor volume 1.356 L. <sup>d</sup> All isomers. <sup>e</sup> 97%  $\text{F}_2$ -propyl chloride plus 33%  $\text{F}_2$ -isopropyl chloride. <sup>f</sup> 13%  $\text{F}_2$ -n-butyl chloride plus 19.8%  $\text{F}_2$ -sec-butyl chloride. <sup>g</sup>  $\text{F}_2$ -isobutyl chloride. <sup>h</sup> mixture, nonphotochemically finished, UV lamp off, nonperfluorinated products. <sup>i</sup> 10.3% 2-chloro-pentane, 15.6% 2-chloro-*n*-pentane, and 6.2% 1-chloro-*n*-pentane.

chloro-*F*-propane matching those published.<sup>28,29</sup>

**Aerosol Fluorination of *n*-Butyl Chloride.** 1-Chlorobutane (Fisher Scientific) was used as received. Its vapor pressure at  $-10^\circ\text{C}$  is such that a flow of 58 mL/min of helium through  $\sim 50$  mL of the material contained in a sparge tube evaporator produces a throughput of 0.29 g/h (3.15 mmol/h). For a 2-h photochemically finished run, 1.1676 g of crude product was collected after vacuum line fractionation. Purification of the products on the GC SE-52 column ( $0^\circ\text{C}/5$  min;  $10^\circ\text{C}/\text{min}$  to  $30^\circ\text{C}$ ;  $25^\circ\text{C}/\text{min}$  to  $180^\circ\text{C}/10$  min) produced 6.9% *F*-*n*-butane ( $t_R = 3$  min) and 60.2% 1-chloro-*F*-butane (compound 1) ( $t_R = 6$  min). The yield of compound 1 based on the calculated throughput was 43.8%. IR ( $\text{cm}^{-1}$ ) 1351 (m), 1285 (sh), 1240 (vs), 1213 (vs), 1160 (w), 1148 (s), 1110 (s), 1020 (sh), 997 (m), 886 (m), 848 (sh), 802 (s), 745 (sh), 732 (s), 694 (m);  $^{19}\text{F}$  NMR (1%  $\text{CFCl}_3/\text{CDCl}_3$ ) (multiplicity, relative area)  $\text{CF}_2^a\text{CF}_2^b\text{CF}_2^c\text{CF}_2^d\text{Cl}$ ,  $\phi_A -81.7$  (qt, 3),  $\phi_B -126.1$  (tm, 2),  $\phi_C -121.6$  (qm, 2),  $\phi_D -68.9$  (tq, 2),  $J_{AB} = J_{AD} = 1.1$  Hz,  $J_{AC} = 9.89$  Hz,  $J_{BD} = 12.64$  Hz,  $J_{CD} = 1.46$  Hz; major mass cations [ $m/e$  (int. formula)], [EI] 237 (25.4,  $\text{C}_4\text{F}_8^{79}\text{Cl}$ ), 235 (77.6,  $\text{C}_4\text{F}_8^{81}\text{Cl}$ ), 219 (100,  $\text{C}_4\text{F}_8$ ), 149 (5.2,  $\text{C}_2\text{F}_4^{79}\text{Cl}$ ), 147 (17.5,  $\text{C}_2\text{F}_4^{81}\text{Cl}$ ), 131 (9.6,  $\text{C}_2\text{F}_4$ ), 119 (12.2,  $\text{C}_2\text{F}_4$ ), 87 (4.4,  $\text{CF}_2^{79}\text{Cl}$ ), 85 (15.2,  $\text{CF}_2^{81}\text{Cl}$ ), 69 (2.7,  $\text{CF}_2$ ).

**Aerosol Fluorination of Isobutyl Chloride.** 1-Chloro-2-methylpropane (Eastman) has a vapor pressure at  $-10^\circ\text{C}$  such that a helium flow of 25 mL/min produces a throughput of 0.18 g/h (1.4 mmol/h). A 2-h run produced 0.3881 g of crude material after fractionation. Separation on the SE-52 column ( $0^\circ\text{C}/5$  min;  $15^\circ\text{C}/\text{min}$ ;  $25^\circ\text{C}/\text{min}$  to  $200^\circ\text{C}/10$  min) gave 15.6% *F*-isobutane ( $t_R = 3$  min), and 78.4% *F*-isobutyl chloride (compound 2) ( $t_R = 6$  min). This corresponds to a 41.6% yield for compound 2. IR ( $\text{cm}^{-1}$ ) 1300 (sh), 1280 (vs), 1195 (s), 1162 (s), 1070 (w), 1042 (m), 988 (s), 916 (m), 863 (s), 751 (m), 722 (ms);  $^{19}\text{F}$  NMR (1%  $\text{CFCl}_3/\text{CDCl}_3$ ) ( $\text{CF}_2^a$ ),  $\text{CF}_2^b\text{CF}_2^c\text{CF}_2^d\text{Cl}$ ,  $\phi_A -73.0$  (td, 6),  $\phi_B -178.5$  (hept  $\times$  d, 1),  $\phi_C -62.0$  (t  $\times$  hept, 2),  $J_{AB} = 10.74$  Hz,  $J_{AC} = J_{BC} = 5.88$  Hz; major mass cations [ $m/e$  (int. formula)] 237 (24.2,  $\text{C}_4\text{F}_8^{79}\text{Cl}$ ), 235 (77.1,  $\text{C}_4\text{F}_8^{81}\text{Cl}$ ), 219 (100,  $\text{C}_4\text{F}_8$ ), 197 (28.8,  $\text{C}_2\text{F}_4^{81}\text{Cl}$ ), 131 (5.1,  $\text{C}_2\text{F}_4$ ), 87 (3.7,  $\text{CF}_2^{79}\text{Cl}$ ), 85 (11.8,  $\text{CF}_2^{81}\text{Cl}$ ).

**Aerosol Fluorination of *sec*-Butyl Chloride.** 2-Chlorobutane (Eastman) has a vapor pressure at  $-10^\circ\text{C}$  such that a helium flow of 33 mL/min produces a throughput of 0.26 g/h (2.8 mmol/h). A 3-h run produces 0.9708 g of crude product after fractionation. Separation on the SE-52 column with the same program as for *F*-*n*-butyl chloride gives two overlapping peaks ( $t_R = 5.5$ –6 min) consisting of (30%) 2-chloro-*F*-butane (compound 3) and (43%) 1-chloro-*F*-butane (compound 1). The calculated yield of compound 1 was 19.5%. The yield of compound 3 was 13.69%;  $^{19}\text{F}$  NMR (1%  $\text{CFCl}_3/\text{CDCl}_3$ )  $\text{CF}_2^a\text{CF}_2^b\text{CF}_2^c\text{CF}_2^d\text{Cl}$ ,  $\phi_A -78.1$  (qt, 3),  $\phi_B -139.2$  (tq, 1),  $\phi_C -121.1$  (qq, 2),  $\phi_D -79.6$  (qd, 3),  $J_{AC} = 10.99$  Hz,  $J_{BD} = 9.77$  Hz,  $J_{AD} = 3.86$  Hz; major mass cations [ $m/e$  (int. formula)] 237 (23.1,  $\text{C}_4\text{F}_8^{79}\text{Cl}$ ), 235 (75.3,  $\text{C}_4\text{F}_8^{81}\text{Cl}$ ), 219 (100,  $\text{C}_4\text{F}_8$ ), 185 (1.6,  $\text{C}_2\text{F}_4^{81}\text{Cl}$ ), 169 (8.4,  $\text{C}_2\text{F}_4$ ), 131 (6.1,  $\text{C}_2\text{F}_4$ ), 119 (7.9,  $\text{C}_2\text{F}_4$ ), 69 (41.8,  $\text{CF}_2$ ).

**Aerosol Fluorination of *tert*-Butyl Chloride.** 2-Chloro-2-methylpropane (Eastman) has a vapor pressure at  $-10^\circ\text{C}$  such that a helium flow of 13 mL/min produces a throughput of 0.28 g/h (3.0 mmol/h). A 2-h run produced 0.8884 g of crude material after fractionation. Separation of the fraction on the SE-52 column with the isobutyl chloride program gave 79.49% *F*-isobutyl chloride (compound 2) ( $t_R = 6$  min) a 46.8% yield of the calculated throughput. No products were found that matched published IR and  $^{19}\text{F}$  NMR spectra of *F*-*tert*-butyl chloride.<sup>30</sup> A second 2-h run with the same throughput and only 8.0 mmol/h fluorine flow and no photochemical finishing gave 0.513 g of partially fluorinated materials. Identifiable compounds produced were 30% unreacted starting material, 30% 1-chloro-2-fluoro-2-methylpropane,<sup>31</sup> 20% 3-chloro-1,2-difluoro-2-methylpropane (compound 4), and 2% 1-chloro-1,2-difluoro-2-methylpropane (compound 5). The yield of compound 4 is 13%;  $^{19}\text{F}$  NMR (1%  $\text{CFCl}_3/\text{CDCl}_3$ ): ( $\text{F}^a\text{CH}_2^b\text{CF}^c(\text{CH}_2^d\text{Cl})(\text{CH}_2^e)$ ),  $\phi_A -244$  (mt, 1),  $\phi_B -185$  (m, 1),  $J_{AB} = 9$  Hz;  $^1\text{H}$  NMR (0.2%  $\text{CHCl}_3/\text{CDCl}_3$ )  $\delta_C$  4.45 (dd, 2),  $\delta_D$  3.65 (dm, 2),  $\phi_B$  1.45 (dd, 3),  $J_{AC} = 47$  Hz,  $J_{BC} = J_{BD} = J_{BE} = 19$  Hz.

(29) Hauptschlein, M.; Braid, M. J. Am. Chem. Soc. 1981, 103, 2363.

(30) Burger, H.; Pawelke, G. Spectrochim. Acta, Part A 1979, 35A, 559.

(31) Olah, G. A.; Bollinger, J. M. J. Am. Chem. Soc. 1968, 90, 947.

## Aerosol Direct Fluorination

J. Org. Chem., Vol. 49, No. 15, 1984 2723

$J_{AB} = J_{AB} = 2$  Hz. The yield of compound 5 is 1.3%:  $^{19}\text{F}$  NMR (1%  $\text{CFCl}_3/\text{CDCl}_3$ )  $\text{CF}_3\text{H}^{\text{C}}\text{ClCF}_2(\text{CH}_2)_3$   $\phi_A$  -144 (md, 1),  $\phi_B$  -187 (m, 1),  $J_{AB} = 9$  Hz;  $^1\text{H}$  NMR (0.2%  $\text{CHCl}_3/\text{CDCl}_3$ )  $\delta_C = 5.95$  (dd, 1),  $\phi_D$  1.45 (md, 6),  $J_{AC} = 56$  Hz,  $J_{BD} = 19$  Hz,  $J_{BC} = 9$  Hz,  $J_{AD} = 2$  Hz.

**Aerosol Fluorination of 1-Chloro-3-methylbutane.** 1-Chloro-3-methylbutane has a vapor pressure at 22 °C such that a helium flow of 12 mL/min produces a throughput of 0.42 g/h (3.0 mmol/h). A 3-h run produced 1.323 g of crude product. Separation on the SE-52 column (15 °C/5 min; 10 °C/min to 75 °C/0 min; 50 °C/min to 160 °C/10 min) gave 19% *F*-isopentane and 67% 1-chloro-*F*-3-methylbutane (compound 6) ( $t_R = 7$  min). The yield of compound 6 is 32%: IR ( $\text{cm}^{-1}$ ) 1300 (sh), 1260 (vs), 1250 (vs), 1225 (vs), 1180 (s), 1145 (m), 1100 (s), 975 (s), 740 (m), 710 (m);  $^{19}\text{F}$  NMR (1%  $\text{CFCl}_3/\text{CDCl}_3$ ) ( $\text{CF}_3$ ) $_2\text{CF}^{\text{B}}\text{CF}_2^{\text{C}}\text{CF}_2^{\text{D}}\text{Cl}$   $\phi_A$  -72.8 (m, 6),  $\phi_B$  -185.7 (m, 1),  $\phi_C$  -113.2 (m, 2),  $\phi_D$  -68.3 (m, 2); major mass cations [ $m/e$  (int. formula)] 287 (10.3,  $\text{C}_6\text{F}_{10}^{77}\text{Cl}$ ), 285 (32.1,  $\text{C}_6\text{F}_{10}^{35}\text{Cl}$ ), 269 (63.4,  $\text{C}_5\text{F}_{10}$ ), 137 (5.8,  $\text{C}_3\text{F}_5^{77}\text{Cl}$ ), 135 (18.7,  $\text{C}_3\text{F}_5^{35}\text{Cl}$ ), 131 (19.2,  $\text{C}_3\text{F}_5$ ), 119 (20.9,  $\text{C}_2\text{F}_4$ ), 100 (11.4,  $\text{C}_2\text{F}_4$ ), 87 (18.5,  $\text{CF}_2^{77}\text{Cl}$ ), 85 (56.7,  $\text{CF}_2^{35}\text{Cl}$ ), 69 (100,  $\text{CF}_2$ ).

**Aerosol Fluorination of 1-Chloro-2-methylbutane.** 1-Chloro-2-methylbutane was reacted under the same conditions as for 1-chloro-3-methylbutane and produced 1.629 g of crude product after fractionation. GC separation gave 19% *F*-isopentane and 66% 1-chloro-*F*-2-methylbutane (compound 7). The yield of compound 7 is 39%: IR ( $\text{cm}^{-1}$ ) 1330 (m), 1270 (sh), 1240 (vs), 1200 (s), 1170 (m), 1140 (m), 1090 (m), 1020 (m), 950 (m), 925 (m), 900 (m), 870 (m), 835 (m), 795 (m), 740 (m), 720 (m);  $^{19}\text{F}$  NMR (1%  $\text{CFCl}_3/\text{CDCl}_3$ ) ( $\text{CF}_3$ ) $_2\text{CF}^{\text{B}}\text{CF}_2^{\text{C}}\text{CF}_2^{\text{D}}\text{Cl}$   $\phi_A$  -60.6 (m, 2),  $\phi_B$  -71.4 (m, 3),  $\phi_C$  -177.0 (m, 1),  $\phi_D$  -117.5 (m, 2),  $\phi_E$  -80.8 (m, 3); major mass cations [ $m/e$  (int. formula)] 287 (15.6,  $\text{C}_6\text{F}_{10}^{77}\text{Cl}$ ), 285 (49.1,  $\text{C}_6\text{F}_{10}^{35}\text{Cl}$ ), 269 (52.0,  $\text{C}_5\text{F}_{10}$ ), 181 (14.5,  $\text{C}_4\text{F}_7$ ), 137 (2.7,  $\text{C}_3\text{F}_5^{77}\text{Cl}$ ), 135 (8.6,  $\text{C}_3\text{F}_5^{35}\text{Cl}$ ), 131 (22.1,  $\text{C}_3\text{F}_5$ ), 119 (42.0,  $\text{C}_2\text{F}_4$ ), 87 (20.7,  $\text{CF}_2^{77}\text{Cl}$ ), 85 (61.2,  $\text{CF}_2^{35}\text{Cl}$ ), 69 (100,  $\text{CF}_2$ ).

**Aerosol Fluorination of 3-Chloropentane.** 3-Chloropentane was prepared by the method of Darzens from 3-pentanol by reaction with  $\text{SOCl}_2$ /pyridine.<sup>32</sup> 3-Chloropentane has a vapor pressure at 28 °C such that a helium flow of 20 mL/min produces a throughput of 0.12 g/h (1.2 mmol/h). A 1.5-h run produced 0.1913 g of crude material after fractionation. Separation on the SE-52 column (15 °C/5 min; 10 °C/min to 75 °C/0 min; 25 °C/min to 160 °C/10 min) gave a mixture of 3-chloro-*F*-pentane (compound 8) (30%), 2-chloro-*F*-pentane (compound 9) (45%), 1-chloro-*F*-pentane (compound 10) (15%,  $t_R = 7$  min). The combined calculated yield is 31%. The IR spectrum of compound 10 matched that published.<sup>33</sup> The  $^{19}\text{F}$  NMR spectra

(1%  $\text{CFCl}_3/\text{CDCl}_3$ ): compound 8  $\text{CF}_3\text{H}^{\text{C}}\text{CF}_2^{\text{B}}\text{CF}^{\text{C}}\text{CF}_2^{\text{D}}\text{CF}_3$   $\phi_A$  -79.0 (d, 3),  $\phi_B$  -120.1 (s, 2),  $\phi_C$  -137.0 (m, 1),  $J_{AC} = 9.2$  Hz, compound 9  $\text{CF}_3\text{H}^{\text{C}}\text{CF}_2^{\text{B}}\text{CF}_2^{\text{C}}\text{CF}_2^{\text{D}}\text{CF}_3$   $\phi_A$  -77.8 (dt, 3),  $\phi_B$  -138.7 (m, 1),  $\phi_C$  -117.6 (m, 2),  $\phi_D$  -124.3 (m, 2),  $\phi_E$  -81.3 (t, 3),  $J_{AC} = 8.2$  Hz,  $J_{AB} = 12.2$  Hz,  $J_{CE} = 4.5$  Hz, compound 10  $\text{CF}_3\text{H}^{\text{C}}\text{CF}_2^{\text{B}}\text{CF}_2^{\text{C}}\text{CF}_2^{\text{D}}\text{CF}_3$   $\phi_A$  -68.6 (t, 2),  $\phi_B$  -120.8 (m, 2),  $\phi_C$  -122.6 (m, 2),  $\phi_D$  -126.7 (m, 2),  $\phi_E$  -81.2 (t, 3),  $J_{AC} = 12.2$  Hz,  $J_{CE} = 12.2$  Hz.

**Aerosol Fluorination of *tert*-Amyl Chloride.** 2-Chloro-2-methylbutane (Eastman) has a vapor pressure at 0 °C such that a helium flow of 53 mL/min produces a throughput of 0.27 g/h (2.5 mmol/h). A 2.5-h run produced 0.9626 g of crude material after fractionation. Separation on the SE-52 column (15 °C/5 min; 10 °C/min to 75 °C; 50 °C/min to 180 °C/10 min) gives 6.2% *F*-isobutane ( $t_R = 3$  min), 22.1% *F*-isopentane ( $t_R = 3.8$  min), and 62.8% of an unresolved mixture (16:6:5:1) ( $t_R = 7$  min), of 1-chloro-*F*-2-methylbutane (compound 7), 1-chloro-*F*-3-methylbutane (compound 5), and 2-chloro-*F*-3-methylbutane (compound 11). No 2-chloro-*F*-2-methylbutane was observed. The  $^{19}\text{F}$  NMR spectrum of compound 11 is (1%  $\text{CFCl}_3/\text{CDCl}_3$ ): ( $\text{CF}_3$ ) $_2\text{CF}^{\text{B}}\text{CF}_2^{\text{C}}\text{CF}_2^{\text{D}}\text{CF}_3$   $\phi_A$  -70.7 (m, 6),  $\phi_B$  -176.0 (m, 1),  $\phi_C$  -135.3 (m, 1),  $\phi_D$  -77.8 (m, 3).

**Aerosol Fluorination of Chlorocyclopentane.** Chlorocyclopentane (Aldrich) has a vapor pressure at -10 °C such that a helium flow of 125 mL/min produces a throughput of 0.21 g/h (2.0 mmol/h). A 3-h run produces 1.30 g of crude product after fractionation. Separation on the QF-1 column (10 °C/13 min; 10 °C/min to 60 °C/5 min; 50 °C/min to 180 °C/5 min) gives 2.6% *F*-butane ( $t_R = 5$  min), 12.5% *F*-cyclopentane ( $t_R = 12$  min), 5%  $\text{C}_5\text{F}_{11}\text{Cl}$  (compounds 1 and 3) ( $t_R = 15$  min), 12.5% *F*-pentane ( $t_R = 18$  min), 49.5% 1-chloro-*F*-cyclopentane (compound 12) ( $t_R = 22$  min), and 15.5% unresolved  $\text{C}_5\text{F}_{11}\text{Cl}$  isomers (compounds 8-10) ( $t_R = 25$ -26 min). The yield of compound 12 is 40.2%: IR ( $\text{cm}^{-1}$ ) 1310 (s), 1275 (m), 1240 (s), 1220 (vs), 1120 (m), 1065 (vw), 1020 (m), 970 (s), 920 (w), 870 (s), 740 (w);  $^{19}\text{F}$  NMR (1%  $\text{CFCl}_3/\text{CDCl}_3$ )  $\phi_{\text{CF}_3}$  -139.8 (m, 1)  $\phi_{\text{CF}_2}$  = -118.0 and -136.5 (AB pattern, 2,5 and 2',5',  $J_{2,5} = J_{2',5'} = 262.5$  Hz, 4)  $\phi_{\text{CF}}$  -126.5 and -129.0 (AB pattern, 3,4 and 3',4',  $J_{3,4} = J_{3',4'} = 253.3$  Hz, 4); major mass cations [ $m/e$  (int. formula)] 199 (31,  $\text{C}_5\text{F}_9^{77}\text{Cl}$ ), 197 (100,  $\text{C}_5\text{F}_9^{35}\text{Cl}$ ), 149 (40,  $\text{C}_4\text{F}_7^{35}\text{Cl}$ ), 131 (56,  $\text{C}_4\text{F}_7$ ), 100 (22,  $\text{C}_4\text{F}_7$ ).

**Acknowledgment.** This work was supported in part by the Office of Naval Research whose support is gratefully acknowledged. Earlier support by the Research Corp. Cottrell Research Fund is also acknowledged.

**Registry No.** 1-Chloropropane, 540-54-6; 1-chlorobutane, 109-69-8; 1-chloro-2-methylpropane, 513-36-0; 1-chloro-3-methylbutane, 107-84-6; 1-chloro-2-methylbutane, 616-13-7; 2-chloro-2-methylpropane, 507-20-0; 2-chloro-2-methylbutane, 594-36-5; 2-chloropropane, 75-29-8; 2-chlorobutane, 78-86-4; 3-chloropentane, 616-20-6; chlorocyclopentane, 930-28-9.

(32) Darzens, G. C. R. *Heb. Seances Acad. Sci.* 1911, 152, 1314.

(33) Hauptschein, M.; Kinsman, R. L.; Grosse, A. V. *J. Am. Chem. Soc.* 1952, 74, 849.